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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/030,464

05/22/2002

Ivo Feussner

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12/19/2005

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EXAMINER

PAK, YONG D

ART UNIT

PAPER NUMBER

1652

DATE MAILED: 12/19/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/030,464

Applicant(s)

FEUSSNER ET AL.

Examiner

Yong D. Pak

Art Unit

1652

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 September 2005.
- 2a) ☒ This action is FINAL. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 12-28 is/are pending in the application.
- 4a) Of the above claim(s) 24-28 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 12-23 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

This application is a 371 of PCT/EP00/06539.

The amendment filed on September 22, 2005, amending claims 12 and 22-23, has been entered.

Claims 12-28 are pending. Claims 24-28 are withdrawn. Claims 12-23 are under consideration.

Response to Arguments

Applicant's amendment and arguments filed on September 22, 2005, have been fully considered and are deemed to be persuasive to overcome the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

The declaration under 37 CFR 1.132 filed on September 22, 2005 is insufficient to overcome the rejection of claims 12-23 based upon the rejection under 35 U.S.C. 103(a) as being unpatentable over Gan et al., Sloane et al. and Geerts et al. as set forth in the last Office action because: see arguments under 35 U.S.C. 103(a).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 12 and claims 13-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 12 recites the phrase "an amino acid sequence of SEQ ID NO:3". The metes and bounds of this phrase in the context of the above claim are not clear to the Examiner. It is not clear whether the polypeptide comprises a fragment of SEQ ID NO:3 or the full length of the amino acid sequence of SEQ ID NO:3. A perusal of the specification did not provide the Examiner with a specific definition for the above phrase. As applicants have not provided a definition for the above phrase, Examiner has interpreted the claims broadly to mean that a lipxygenase comprising "an amino acid of SEQ ID NO:3" encompasses fragments of SEQ ID NO:3. Examiner requests clarification of the above phrase and suggests amending the claim by replacing "an" with "the" in the above phrase.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 12-23 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 12-23 are drawn to a method enhancing the specificity of a potato tuber lipoxygenase by modifying "at least one" (however the phrase does not limit the change to only one amino acid) amino acid of a wild type potato tuber lipoxygenase including substituting residue 576 of SEQ ID NO:3, a mutant potato tuber lipoxygenase obtained by said method, a polynucleotide encoding said variant, and a vector and host cell comprising said polynucleotide. Since the method modifies one to 857 amino acids of any wild type potato tuber lipoxygenases, including many different lipoxygenases belonging to the class of lipoxygenases, the claims encompass a method of modifying a wild type potato tuber lipoxygenase by changing any number of amino acids not limited to only residue 576, a mutant lipoxygenase obtained from said method, and polynucleotides encoding said lipoxygenase. Therefore, the claims are drawn to a method of modifying any amino acids in a genus comprising any wild type potato tuber lipoxygenase having any structure which results in a genus comprising mutant potato tuber lipoxygenase having any structure and a genus comprising polynucleotides encoding a potato tuber lipoxygenase having any structure. The specification only describes a method of increasing specificity towards position 11 of arachidonic acid by modifying a potato tuber 5-lipoxygenase having the amino acid sequence of SEQ ID NO:3 with a specific substitution at position 576, a variant of a potato tuber 5-lipoxygenase of SEQ ID NO:3 consisting of a substitution at position 576 and a polynucleotide encoding said mutant. However, these examples are not enough to describe the structure and more importantly do not constitute a representative number of species to describe the whole genus and there is no evidence on the record of the

Art Unit: 1652

relationship between the structure of the claimed variant and the structure of any or all mutants of any wild type potato tuber lipoxygenase, which includes any potato tuber lipoxygenase belonging to the class of lipoxygenases. Therefore, the specification fails to describe the structure of species of a genus comprising a method of enhancing the specificity of any wild type potato tuber lipoxygenase by modifying any amino acids, a genus comprising such mutant potato tuber lipoxygenase obtained and a genus comprising a polynucleotide encoding said mutant potato tuber lipoxygenase.

Given this lack of description of the representative species encompassed by the genus of the claims, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the inventions of claims 12-23.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

In response to the previous Office Action, applicants have traversed the above rejection. Applicants argue that since the claims have been amended to recite a method of enhancing the specificity of a potato tuber lipoxygenase by changing "at least one amino acid" in a wild potato tuber lipoxygenase, the claims meet the written description requirements. Examiner respectfully disagrees. Contrary to applicants' arguments, the claims do not recite the limitation that the wild type potato tuber lipoxygenase comprises the amino acid sequence of SEQ ID NO:3. The claims are drawn to a method of modifying any wild type potato tuber lipoxygenases, which

Art Unit: 1652

includes any lipoxygenases belonging to the class of lipoxygenase, including but not limited to E.C. 1.13.11.12, 1.13.11.31, 1.13.11.33, 1.13.11.34, 1.13.11.40 or 1.13.11.45 (see Exapsy: lipoxygenase – form PTO-892). Further, the phrase “at least one” is an open phrase and could mean that just one or any number of amino acids of a potato tuber lipoxygenase, in conjunction with residue 576, can be modified. Therefore, the rejection is maintained.

Claims 12-23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of increasing specificity of a potato tuber 5-lipoxygenase having the amino acid sequence of SEQ ID NO:3 towards position 11 of arachidonic acid by substituting position 576, a variant of a potato tuber 5-lipoxygenase of SEQ ID NO:3 consisting of the substitution at position 576 and a polynucleotide encoding said above potato tuber 5-lipoxygenase variant, does not reasonably provide enablement for a method of modifying any amino acids in any wild type potato tuber lipoxygenase, a mutant lipoxygenase obtained from said method, and polynucleotides encoding said lipoxygenase. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required are summarized in In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir. 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4)

Art Unit: 1652

the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

Claims 12-23 are drawn to a method enhancing the specificity of a potato tuber lipoxygenase by modifying "at least one" (however the phrase does not limit the change to only one amino acid) amino acid of a wild type potato tuber lipoxygenase including substituting residue 576 of SEQ ID NO:3, a mutant potato tuber lipoxygenase obtained by said method, a polynucleotide encoding said variant, and a vector and host cell comprising said polynucleotide. Since the method modifies one to 857 amino acids of any wild type potato tuber lipoxygenases, including many different lipoxygenases belonging to the class of lipoxygenases, the claims encompass a method of modifying a wild type potato tuber lipoxygenase by changing any number of amino acids not limited to only residue 576, a mutant lipoxygenase obtained from said method, and polynucleotides encoding said lipoxygenase. Therefore, the claims are drawn to a method of modifying any amino acids in any wild type potato tuber lipoxygenase having any structure which results in a mutant potato tuber lipoxygenase having any structure and polynucleotides encoding a potato tuber lipoxygenase having any structure.

The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polynucleotides and polypeptides encompassed by the claims. Since the encoded amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired

Art Unit: 1652

activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to a method of increasing specificity towards position 11 of arachidonic acid by modifying a potato tuber 5-lipoxygenase having the amino acid sequence of SEQ ID NO:3 with a substitution at position 576, a variant of a potato tuber 5-lipoxygenase of SEQ ID NO:3 consisting of a substitution at position 576 and a polynucleotide encoding said mutant.

It would require undue experimentation of the skilled artisan to make and use the claimed polynucleotides and polypeptides and enhance specificity of any wild type potato tuber lipoxygenase by modifying any amino acids other than modifying the 5-lipoxygenase of SEQ ID NO:3 with an amino acid substitution at position 576. The specification provides no guidance with regard to the making of other variants and mutants or with regard to other uses. In view of the great breadth of the claims, amount of experimentation required to make the claimed polypeptides and polynucleotides, the lack of guidance, working examples, and unpredictability of the art in predicting function from a polypeptide primary structure, the claimed invention would require undue experimentation. As such, the specification fails to teach one of ordinary skill how to use the full scope of the polynucleotides and polypeptides encompassed by the claims.

While enzyme isolation techniques, recombinant and mutagenesis techniques are known, and it is routine in the art to screen for multiple substitutions or multiple

Art Unit: 1652

modifications as encompassed by the instant claim, the specific amino acid positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass modifying any amino acids in any wild type potato tuber lipoxygenase and mutant potato tuber lipoxygenase and polynucleotides encoding said lipoxygenase obtained from such method, because the specification does not establish: (A) regions of the polypeptide structure, other than a substitution at position 576 in SEQ ID NO:3, which may be modified without affecting lipoxygenase activity or 5-lipoxygenase activity; (B) specific amino acids in the polypeptide structure which may be modified resulting in enhanced substrate specificity towards position 11 of arachidonic acid; (C) the general tolerance of lipoxygenase to modification and extent of such tolerance; (D) a rational and predictable scheme for modifying any amino acid residue with an expectation of obtaining the desired biological function; and (E) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including a method of enhancing specificity of any

Art Unit: 1652

wild type potato tuber lipoxygenase by modifying any amino acids and mutant lipoxygenases and polynucleotides encoding said lipoxygenase obtained from such method. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of polypeptides comprising any variants, mutants and recombinants of any potato tuber lipoxygenase having enhanced substrate specificity is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

In response to the previous Office Action, applicants have traversed the above rejection. Applicants argue that since the claims have been amended to recite a method of enhancing the specificity of a potato tuber lipoxygenase by changing at least one amino acid in a wild potato tuber lipoxygenase, the claims meet the enablement requirements. Examiner respectfully disagrees. Contrary to applicants' arguments, the claims do not recite the limitation that the wild type potato tuber lipoxygenase comprises the amino acid sequence of SEQ ID NO:3 and the modification limited to amino acid 576. The claims are drawn to a method of modifying any wild type potato tuber lipoxygenases, which includes any lipoxygenases belonging to the class of lipoxygenase, including but not limited to E.C. 1.13.11.12, 1.13.11.31, 1.13.11.33, 1.13.11.34, 1.13.11.40 or 1.13.11.45 (see Exapsy: lipoxygenase – form PTO-892). Further, the phrase “at least one” is an open phrase and could mean that just one or

Art Unit: 1652

any number of amino acids of a potato tuber lipoxygenase, in conjunction with residue 576, can be modified. Therefore, the rejection is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 12-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gan et al., Sloane et al. and Geerts et al.

Claims 12-23 are drawn to a method of enhancing a wild type potato plant lipoxygenase towards position 11 of arachidonic acid by substituting the residue at 576, a potato lipoxygenase variant comprising a substitution corresponding to position 576

and a polynucleotide encoding said variant. Examiner notes that the patentability of a product does not depend on the method used in producing the product (MPEP 2113).

Gan et al. (form PTO-892) discloses that Phe at position 557 of a soybean 1-lipoxygenase and Met at position 418 of a human lipoxygenase are critical for substrate binding and effects positional specificity of arachidonic acid (abstract, pages 25412-25413). Sloane et al. (form PTO-892) discloses site directed mutagenesis at position 418 of human lipoxygenase changes the enzyme's substrate specificity. A sequence alignment of Accession number S73865 and the sequences of Sloane et al. and Gan et al. shows that amino acid 418 of human lipoxygenase and amino acid 557 of soybean lipoxygenase, correspond to position 576 of a potato tuber 5-lipoxygenase (See sequence alignment).

The difference between the references of Gan et al. and Sloan et al. and the instant invention is that the references do not teach a method of enhancing the specificity of a potato tuber lipoxygenase for position 11 of arachidonic acid by substituting residue 576 with a Phe residue, or a potato tuber lipoxygenase variant comprising a substitution at residue 576 or a polynucleotide encoding said variant.

Geerts et al. (form PTO-892) discloses a polynucleotide encoding a potato tuber 5-lipoxygenase having an accession number S73865 in the EMBL database (page 272). Gerets et al. also discloses a vector and host cell comprising said polynucleotide (page 270).

Therefore, combining the teachings of the above three references, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was

Art Unit: 1652

made to mutagenize the lipoxygenase of Geerts et al. at position 576. One of ordinary skill in the art would have been motivated to mutagenize the lipoxygenase of Geerts et al. in order to alter the enzyme's positional specificity of arachidonic acid. One of ordinary skill in the art would have had a reasonable expectation of enhancing the enzyme's positional specificity of position 11 of arachidonic acid since Gan et al. and Sloane et al. teach that the residue corresponding to position 576 of potato tuber lipoxygenase is critical for substrate binding and effects positional specificity of arachidonic acid.

Therefore, Gan et al., Geerts et al. and Sloane et al. render claims 12-23 *prima facie* obvious to those skilled in the art.

In response to the previous Office Action, applicants have traversed the above rejection.

Applicants argue that one of ordinary skill in the art would not expect that modifying the amino acids of a potato tuber lipoxygenase that correspond to position 418 of a human lipoxygenase would enhance the specificity of the potato tuber lipoxygenase for position 11 of arachidonic acid and therefore claims 12-23 are not obvious over Gan et al., Geerts et al. and Sloane et al. Examiner respectfully disagrees. Although Gan et al. and Sloane et al. does not teach enhancing a potato tuber lipoxygenase's specificity for position 11 of arachidonic acid, Gan et al. and Sloane et al. does teach that the residue 418 of a human lipoxygenase, which corresponds to position 576 of potato tuber lipoxygenase, is critical for substrate binding and effects positional specificity of arachidonic acid. Based on this observation, one

Art Unit: 1652

having ordinary skill in the art would have been motivated to modify other lipoxygenase by substituting the amino acid corresponding to 418 of human lipoxygenase. Applicants have filed a declaration under 37 CFR 1.132 arguing mutation at position 576 of a potato tuber lipoxygenase results in a lipoxygenase having enhanced specificity towards position 11 of arachidonic acid instead of position 12. However, MPEP 2144 states that

“The reason or motivation to modify the reference may often suggest what the inventor has done, but for a different purpose or to solve a different problem. It is not necessary that the prior art suggest the combination to achieve the same advantage or result discovered by applicant... while there must be motivation to make the claimed invention, there is no requirement that the prior art provide the same reason as the applicant to make the claimed invention.”

In the instant case, since the references of Gan et al., Sloane et al. and Geerts et al. in combination provides a suggestion and motivation of modifying an amino acid corresponding to residue at position 576 of SEQ ID NO:3, which is to modify the enzyme's specificity towards arachidonic. Further, there is a reasonable expectation of success, since Gan et al. and Sloane et al. teaches that the residue corresponding to position 576 of potato tuber lipoxygenase is critical for substrate binding and effects positional specificity of arachidonic acid. Therefore, Gan et al., Geerts et al. and Sloane et al. render claims 12-23 *prima facie* obvious to those skilled in the art.

Applicants also argue that Office Action has contradicted itself for alleging that one of ordinary skill in the art would not be able to identify amino acid residues in other plant lipoxygenase that correspond to amino acid 576 of a potato tuber lipoxygenase in the enablement rejection yet in the obviousness rejection, Office Action contends that one of ordinary skill in the art would be able to determine which amino acid at position

Art Unit: 1652

576 of a potato tuber lipoxygenase. Examiner respectfully disagrees. Such statement was not made in the enablement rejection. The earlier enablement rejection argued that the specification was not enabled for “a method of enhancing specificity of any plant lipoxygenase, any plant lipoxygenase variant comprising a substitution at position 576 or a polynucleotide encoding any plant lipoxygenase variant comprising a substitution at position 576” (page 8 of the Office Action mailed on May 20, 2005). The previous rejection was altered. However, applicants have only now limited the enzymes to Potato tuber. Furthermore, Examiner has argued that the specific position 576 would be obvious to modify not in any or all amino acid positions. In the current enablement rejection, Examiner agrees that claims are enabled for the lipoxygenase of SEQ ID NO:3 consisting of the specific mutation at position 576. Therefore, as opposed to applicants argument, Examiner’s enablement rejection and the obviousness rejection are not contradictory.

Hence, the rejection is maintained.

None of the claims are allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

Art Unit: 1652

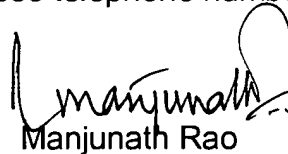
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong Pak whose telephone number is 571-272-0935. The examiner can normally be reached 6:30 A.M. to 5:00 P.M. Monday through Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone numbers for the organization where this application or proceeding is assigned are 571-273-8300 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Yong D. Pak
Patent Examiner 1652

A handwritten signature in black ink, appearing to read "Manjunath Rao", with a stylized flourish at the end.

Manjunath Rao
Primary Patent Examiner 1652